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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/763,299	01/22/2004	Jennifer K. Fredrickson	00538/1	6538

7590 04/16/2007  
Karen B. King  
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EXAMINER
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SASAN, ARADHANA

ART UNIT	PAPER NUMBER
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1609

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/16/2007	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/763,299	<b>Applicant(s)</b> FREDRICKSON ET AL.	
	<b>Examiner</b> Aradhana Sasan	<b>Art Unit</b> 1609	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 29 March 2007.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-50 is/are pending in the application.
- 4a) Of the above claim(s) 35-50 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-34 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 22 January 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>08/27/204 &amp; 08/30/2004</u> . | 6) <input type="checkbox"/> Other: _____  |

***DETAILED ACTION***

1. Receipt is acknowledged of applicant's response to Restriction Requirement filed on March 29, 2007.

**Status of Application**

***Election/Restrictions***

2. Applicant's election with traverse of Group I (claims 1-34) in the reply filed on March 29, 2007 is acknowledged. The traversal is on the ground(s) that the search and examination of hydrophobic polymer film species and viscosity enhancing substances can be made without serious burden using standard electronic search methods. This is not found persuasive because the search for the generic class of substances does not necessarily yield all the species listed in the claim. In the Sparks et al. (US 5,354,556) reference, the hydrophobic polymer film species vinyl carbonate, vinylidene, or acrylonitrile copolymers, and viscosity enhancing substances microcrystalline cellulose and carboxymethylcellulose are not listed. The search for the species would be a separate search.

The election of specie requirement is still deemed proper and is therefore made FINAL.

3. Claims 35-50 are withdrawn.
4. Claims 1-34 are being presented for examination.

***Information Disclosure Statement***

5. The information disclosure statements (IDS) submitted on 08/27/2004 and 08/30/2004 were filed. The submissions are in compliance with the provisions of 37

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CFR 1.97 and 1.98. Accordingly, the examiner is considering the information disclosure statements.

See attached copy of PTO-1449.

### ***Specification***

6. The disclosure is objected to because of the following informalities: There is a typo on page 23, [00105]; "sink" is mistyped as "sin". Appropriate correction is required.

### ***Claim Objections***

7. Claim 30 is objected to because it depends on "claim 30". Since claim 30 recites a limitation of "at least one taste-masking substance" which is recited in claim 29, claim 30 should depend on claim 29. Appropriate correction is required.

### ***Double Patenting***

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claims 1-34 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8, 10-11, 15-16, 20-26 of copending Application No. 10/790,312 ('312 hereafter). Although the conflicting claims are not identical, they are not patentably distinct from each other.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Regarding the claim limitations of instant claim 1, '312 claims a dry formulation of coated linezolid, which can be suspended in an aqueous solution, and is taste masked. Claim 1 in '312 discloses "at least one dose" whereas instant claim 1 discloses "at least two doses". It would have been obvious to one skilled in the art to modify the formulation parameters to increase or decrease the doses included. The particle size (50 $\mu$ m-600 $\mu$ m) claim limitation is also disclosed in claim 11 of '312. The hydrophobic polymer claim limitation is also disclosed in claim 7 of '312. The viscosity enhancing substance claim limitation is also disclosed in claim 22 of '312. The claim limitations of the suspension time, volume of liquid per dose, and mixing in the presence of air would have been obvious to one skilled in the art because by modifying the formulation parameters one could achieve the desired viscosity, suspendability, release, and stability.

The limitations of instant claims 2-3, and 23-24 (hydrophobic polymers and methacrylic acid as the elected species) are also disclosed in claims 7-8 of '312.

The plasticizer of instant claims 4 and 25 is disclosed as the surfactant in claim 10 of '312.

The oxazolidinone and linezolid of instant claims 5-6, and 26-27 are disclosed in claims 2 and 3 of '312.

Xanthan gum and carboxymethyl cellulose and crystalline cellulose of instant claims 7-8, and 28, are disclosed in claim 22 of '312.

The particle size (100 $\mu$ m-600 $\mu$ m) of instant claim 12 is included in the range (50 $\mu$ m-600 $\mu$ m) disclosed in claim 11 of '312.

The taste masking substance (sucrose) of instant claims 13-15, and 29-31, is disclosed in claims 15-16 of '312.

The flavoring of instant claims 17 and 33 is disclosed in claim 20 of '312.

Water as the aqueous liquid from instant claim 18 is disclosed in claim 26 of '312.

Suspension time within 5 minutes of instant claim 19 is included in claim 25 of '312 (which discloses that suspension is facilitated "in less than about three (3) minutes after addition of the aqueous solution to the dry formulation" (Page 15, claim 25)).

Regarding instant claims 9-11 and 21, the weight ratio of xanthan gum to the combination of microcrystalline cellulose and sodium carboxymethylcellulose and the viscosity of the suspension would have been obvious variants to one skilled in the art because a person skilled in the art would modify the weight ratio of the composition (and consequently the suspension viscosity) based on the required release profile, suspendability, and stability. The recited weight ratios and viscosity values are obvious variants unless there is evidence of criticality or unexpected results.

The viscosity range of instant claim 22 would also be obvious to one skilled in the art given the reasoning for instant claim 21.

The artificial sweetener as a taste-masking agent of instant claims 16 and 32 would have been obvious to one skilled in the art as alternative means of taste masking unpleasant tasting active ingredients.

Given the formulation of microencapsulated linezolid, viscosity enhancing substances, and the resulting suspension after adding the dry formulation to an aqueous liquid such as water, the limitations of instant claims 20 and 34 regarding the homogeneous dispersion of air bubbles and solid particles would be obvious to one skilled in the art.

Since the instant application claims a dry formulation of coated drug particles and a viscosity enhancing substance, which will remain in suspension, it is obvious over the claims of copending application '312 and thus, they are not patentably distinct over each other.

***Claim Rejections - 35 USC § 102***

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 1-4, 7, 13-15, 18, and 20 are rejected under 35 U.S.C. 102(b) as being anticipated by Sparks et al. (US 5,354,556).

The claimed invention is a dry formulation comprising at least two doses of coated drug particles and a viscosity enhancing substance in an amount effective to

maintain the doses of coated drug in suspension (substantially homogenous) for at least 24 hours after combination with an aqueous liquid and mixing in the presence of air.

Sparks teaches a controlled release powder containing microparticles, which can be readily formulated in liquid form (Col. 1, lines 44-46). The microparticles have an average particle size of from 0.1 to 125  $\mu\text{m}$  (Col. 1, lines 59-60). The microparticles contain an active ingredient that is not entirely coated by the non-toxic polymer (Col. 22, lines 10-21, claim 1). The powder can be "suspended in a liquid vehicle and will maintain its sustained release characteristics for a useful period of time. These dispersions or suspensions have both chemical stability and stability in terms of dissolution rate" (Col. 3, lines 21-25).

Sparks teaches polymers of acrylic and methacrylic acids (Col. 3, lines 35-36).

The use of xanthan gum as a thickening agent to increase the viscosity is taught (Col. 6, lines 51-53). Polyoxyethylene sorbitan ester as an excipient used in association with the active ingredient is taught (Col. 7, lines 28-35). The oral suspensions using the polymer coated active ingredient masks the unpleasant taste (Col. 8, lines 24-26). Antibiotic suspensions are included in the preferred suspensions (Col. 8, lines 31-35). The "liquids offer versatility and the possibility of twice daily administration of a medicament..." (Col. 8, lines 52-56).

This reference also teaches "controlled release antibiotic formulations substantially free from the taste of the antibiotic for pharmaceutical or veterinary use" (Col. 1, lines 61-68). Sugar is used as the taste-masking compound (Col. 22, lines 42-44, claim 6).



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Water as a suitable liquid for the suspension is taught (Col. 6, lines 48-49).

Regarding instant claim 1, Sparks anticipates the claim limitation of "at least two doses" because the suspensions offer the possibility of twice-daily administration of a medicament. The claim limitation of maintaining the suspension for "at least 24 hours at about 20°C to about 30°C" is anticipated by Sparks because in the stability study of the suspension, samples were stored at room temperature and tested at 1, 2, 3, 4, 5, 6, and 24 hour time intervals over a period of 15 weeks (Col. 15, lines 33-42, and lines 56-67). Room temperature can reasonably be thought of as "about 20°C to about 30°C". The claim limitation of "about 2ml to about 60ml of an aqueous liquid per dose" is anticipated by Sparks because several examples included in this reference include 5ml suspensions per dose of active (300mg of acetaminophen per 5ml in example 15). A person skilled in the art could readily envisage a suitable volume of the suspension vehicle to ensure the dosage, suspendability, release, and stability of the active is maintained.

Regarding instant claim 4, Sparks anticipates the claim limitation of the plasticizer because a polyoxyethylene sorbitan ester is taught. A person skilled in the art can envisage this surfactant as a plasticizer.

Regarding instant claim 7, Sparks anticipates the claim limitation of xanthan gum (elected species) because this reference teaches xanthan gum as a viscosity enhancing substance (mentioned above).

Regarding instant claims 13-15, Sparks anticipates the claim limitation of using sugar as a taste masking substance (mentioned above).

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Sparks anticipates instant claim 20, because the reference teaches suspensions that demonstrate bioavailability and dissolution rate stability over a period of time. A person skilled in the art would clearly envisage a drug suspension with demonstrated bioavailability and stability as a suspension having a homogenous dispersion of air bubbles and solid particles.

***Claim Rejections - 35 USC § 103***

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

13. Claims 5-6 rejected under 35 U.S.C. 103(a) as being unpatentable over Sparks et al. (US 5,354,556).

Instant claims 5 and 6 would have been obvious to one skilled in the art because Sparks teaches "controlled release antibiotic formulations substantially free from the taste of the antibiotic for pharmaceutical or veterinary use" (Col. 1, lines 61-68). Since claims 5 and 6 recite the drug linezolid (an oxazolidinone antibiotic), a person skilled in the art would have found it obvious that the delivery of the antibiotic linezolid would benefit from a taste masking, controlled release formulation as taught by the antibiotic formulation of Sparks.

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14. Claims 8-12, 16-17, 19, and 21-34 rejected under 35 U.S.C. 103(a) as being unpatentable over Sparks et al. (US 5,354,556), in view of Zema et al. (US 5,306,506).

The teaching of Sparks is stated above.

Sparks does not teach microcrystalline cellulose and sodium carboxymethylcellulose and flavoring or the time it takes the coated drug particles to be suspended in the aqueous liquid.

Zema teaches a solid pharmaceutical composition for addition to water to produce a suspension of a drug (Abstract). Microcapsules of drugs are taught (Col. 1, lines 5-9). Zema further teaches a "thickening agent, which in 15-20 seconds confers sufficient viscosity to the medium to maintain the microcapsules in a homogenous suspension in order to avoid the formation of lumps and especially separation of the microcapsules" (floating and sedimentation) (Col. 4, lines 25-35). The thickening substances include "xanthan gum, ... carboxymethyl cellulose, crystalline cellulose alone or in combination with other hydrocolloids (e.g. AVICEL RC-591 of FMC Corporation)" (Col. 5, lines 20-26). It would have been obvious to one of ordinary skill in the art to add microcrystalline cellulose and carboxymethylcellulose to the composition of Sparks, as claimed in instant claim 8. The motivation to do so would be to use alternate thickening or viscosity enhancing substances such as microcrystalline cellulose and carboxymethylcellulose in addition to xanthan gum during routine optimization of suspension formulations. An added motivation is provided by the time it takes to suspend the particles in an aqueous liquid and is taught by Zema (Col. 4, lines 25-35).

Flavoring is also used with the composition (Col. 5, lines 59-64).

It would have been obvious to a person skilled in the art to combine the teachings of Sparks and Zema to arrive at the claimed invention. The motivation to combine the two references is provided by the fact that linezolid is an antibiotic and Sparks teaches taste-masked antibiotic formulations. Similarly, adding artificial sweeteners that are commercially available, along with flavors to mask the unpleasant taste of the active would have been obvious to a person skilled in the art.

Instant claim 8 would have been obvious to a person having ordinary skill in the art at the time the invention was made given the teaching of Sparks in view of Zema since Zema teaches xanthan gum, microcrystalline cellulose, and carboxymethylcellulose.

Regarding instant claims 9-11, and 21-22, the weight ratio of xanthan gum to the microcrystalline cellulose and carboxymethylcellulose, and the suspension viscosity would have been obvious given the teaching of Sparks in view of Zema. A person skilled in the art would modify the weight ratio of the composition (and consequently the suspension viscosity) based on the required release profile, suspendability, and stability, and the recited weight ratios are obvious variants unless there is evidence of criticality or unexpected results.

Instant claims 16 and 17 would have been obvious to one skilled in the art in given the teaching of Sparks in view of Zema. Since the antibiotic requires taste masking (taught by Sparks), one skilled in the art would use sugars, intense or artificial sweeteners, and flavoring in order to mask the off-taste of the active.

Instant claim 19 would have been obvious to one skilled in the art given the teaching of Sparks in view of Zema. Zema teaches that when the composition is mixed with water a homogeneous suspension of the drug is obtained within 30 seconds (Abstract).

Instant claims 23-34 would have been obvious to one skilled in the art given the teaching of Sparks in view of Zema, since Zema provides the elements of the viscosity enhancing substances microcrystalline cellulose and carboxymethylcellulose that are missing from the Sparks teaching.

### ***Conclusion***

1. No claims are allowed.
2. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aradhana Sasan whose telephone number is (571) 272-9022. The examiner can normally be reached Monday to Thursday from 6:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang, can be reached at 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should

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JANET L. ANDRES  
SUPERVISORY PATENT EXAMINER

